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10/089,362	01/14/2003	David Elsley	033136-269	7852

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EXAMINER	
HENLEY III, RAYMOND J	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 02/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,362	ELSLEY, DAVID	
	Examiner	Art Unit	
	Raymond J Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-48* is/are rejected.

7)☒ Claim(s) *23,25,32-41 and 45-47* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/29/02 & 3/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 21-48 ARE PRESENTED FOR EXAMINATION

Applicant's Preliminary Amendment filed April 17, 2003 and Information Disclosure Statements filed August 29, 2002 and March 1, 2004 have been received and entered into the application.

Accordingly, claims 1-20 have been canceled and claims 21-48 have been added. Also, as reflected by the attached, completed copies of form PTO-1449 (3 pages), the Examiner has considered the cited references.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on the applications filed in Canada on September 24, 1999 and September 28, 1999. Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath, declaration or application data sheet does not acknowledge the filing of any foreign application. A new oath, declaration or application data sheet is required in the body of which the present application should be identified by application number and filing date.

Claim Objections

Claims 23, 25 and 32-41 and 45-47 are objected to because of the following informalities:

(i) in claims 23, 32-41 and 45-47, "the cholesterol modifying" and "the cholesterol-lowering" does not have antecedent basis in preceding claims (it is suggested that these terms be incorporated in the preceding claims to comport with the language employed throughout the present specification at pages 1-23); and

(ii) in claim 25, "the patient" does not have antecedent basis, i.e., claim 21 recites "a/the mammal".

Appropriate correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

In the specification as originally filed, page 13, line 8, it is set forth "In respect of cerivastatin, an entirely synthetic compound, the most appropriate daily dosage is much lower, namely from about 0.1 - 0.8 mg.". Further, at page 18, line 10, a dosage of 0.5 mg is indicated for cerivastatin.

In present claim 37, however, which was added by amendment on April 17, 2003, the dosage for cerivastatin is stated to be "from about 5 to about 200 mg." which is clearly not

supported by the disclosure in the specification as originally filed and thus represents new matter which is not permissible (see 35 U.S.C. § 132 and 37 CFR § 1.121).

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set for the claimed invention. *Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Considering the teachings provided by Applicant in the specification as originally filed, the Examiner finds that Applicant has failed to provide the necessary teaching, by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formula that fully set forth the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that cerivastatin could or should be administered at a daily dosage of from about 5 to about 200 mg.

Accordingly, claim 37 is deemed properly rejected under 35 U.S.C. § 112, first paragraph.

Suggestion for Overcoming the Above Rejection

Applicant may wish to consider amending claim 37 by changing "about 5 to about 200 mg" to ---0.1 - 0.8 mg--- in order to overcome this rejection.

It is noted in the present specification that the term "about" precedes "0.1 – 0.8 mg". The recitation of such in the claims, however, would raise an issue under 35 U.S.C. § 112, second paragraph because the present specification does not provide any indication as to what range is covered by the term "about", i.e., "about 0.1 – 0.8 mg" would be indicative of an undefined range of amounts that is almost or approximately a range of from 0.1 – 0.8 mg (also see below under the heading "Claim Rejection, 35 U.S.C. § 112, second paragraph").

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-41 and 45-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of atherosclerosis in a patient being treated with a lipid profile modifying/lowering drug, does not reasonably provide enablement for the treatment, in general, of a patient being treated with a lipid profile modifying/lowering drug. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The present claims lack a recitation of a therapeutic objective to be achieved through the administration of a lipid profile modifying/lowering drug to a mammal. Therefore, the claims encompass the treatment of the host for *any* therapeutic purpose. The art, however, is currently unaware of any agent, or combination of agents, which is effective for treating all disease conditions, i.e., a panacea. Lacking knowledge of such, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation that all disease conditions could be treated in a mammal taking a lipid profile modifying/lowering drug. Given that the art fails to recognize, and Applicant has failed to demonstrate, that all disease conditions could be treated in a mammal being administered a lipid modifying/lowering drug, the skilled artisan would be faced with the impermissible burden of undue experimentation in order to practice this embodiment of the claimed invention.

Suggestion for Overcoming the Above Rejection

In order to overcome the above rejection, Applicant should amend claim 1 (and make any further amendments to the dependent claims as necessary) so as to read:

---In a method of treating atherosclerosis in a mammalian subject which comprises administering an effective amount of a cholesterol-lowering drug thereto wherein the improvement comprises...---.

Claim Rejection - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25 and 31-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "about" in these claims, e.g., "about 0.1 to about 100 ml" (claim 25), is a relative term which renders the claim indefinite. The expression "about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and thus one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, because there is no objective standard or definition for the term "about", it is unclear whether or not which, if any, blood volumes of 111 ml, 115 ml, 120 ml, 200 ml or 500 ml are within or outside of the scope of present claim 25.

"The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what

constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph with respect to the claimed invention." (MPEP 2173).

Because the term "about" is not defined in the present specification, such would invite arbitrary and/or subjective interpretations of whether or not a particular volume of blood, period of time or dosage amount is included by or excluded from the present claims and it is the Examiner's position that the public would not be informed of the boundaries of what constitutes infringement of the present claims. Thus, the claims do not meet the requirements of 35 U.S.C. § 112, second paragraph.

Jepson-Type Claims

Applicant's claims 21-41 and 38-43 are drafted in Jepson format (see 37 C.F.R. § 1.175(e)). Therefore, and in the absence of a disclosure by Applicant to the contrary, the subject matter of the preamble, i.e., "In a method of treating a mammal subject with a lipid profile modifying drug" (claim 21), "the mammalian subject suffers from atherosclerosis" (claim 22), etc., is taken as an implied admission that such is prior art work of another (see MPEP § 2129 (III)). Also, that which is recited in the preamble of a Jepson style claim cannot ordinarily be relied upon to distinguish over the prior art. See *In re Skrivan*, 166 U.S.P.Q. 85, (CCPA 1970).

Multiple Reference 35 U.S.C. § 102 Rejection

This Office action a rejection under 35 U.S.C. § 102 based on multiple references. The additional reference is relied on to explain the meaning of a term used in the primary reference or to show that a characteristic not disclosed in the primary reference is inherent. Accordingly, the

Examiner's reliance on multiple references is proper. "Normally, only one reference should be used in making a rejection under 35 U.S.C. § 102. However, a 35 U.S.C. § 102 rejection over multiple references has been held to be proper when the extra references are cited to:

(A) Prove the primary reference contains an "enabled disclosure;"

(B) Explain the meaning of a term used in the primary reference; or

(C) Show that a characteristic not disclosed in the reference is inherent." (See MPEP § 2131.01).

Legal Standard for Anticipation/Inherency Under - 35 USC § 102

To anticipate a claim under 35 U.S.C. § 102, a single prior art reference must place the invention in the public's possession by disclosing each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to practice the invention. *Scripps Clinic & Research Foundation v. Genetech, Inc.,* 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1001 (Fed. Cir. 1991); *In re Donahue,* 766 F2d531, 533, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). To anticipate, the prior art must either expressly or inherently disclose every limitation of the claimed invention. *MEHL/Biophile Int'l Corp. v. Milgraum,* 192 F.3d 1362, 1365, 52 U.S.P.Q.2d 1303, 1303 (Fed. Cir. 1999) (citing to *In re Schreiber,* 128 F.3d 1473, 1477, 44 U.S.P.Q. 1429, 1431 (Fed. Cir. 1997)); *Atlas Powder Co. v. Ireco Inc.,* 190 F.3d 1342, 1347, 51 U.S.P.Q.2d 1943, 1946 (Fed. Cir. 1999). To inherently anticipate, the prior art must necessarily function in accordance with, or include, the claimed limitations. *MEHL/Biophile,* 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. However, it is not required that those of ordinary skill in the art recognize the inherent characteristics or the function of the prior art. *Id.* Specifically, discovery

of the mechanism underlying a known process does not make it patentable.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21, 22, 38, 42-44 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Bisaccia et al. (U.S. Patent No. 5,426,116, cited by the Examiner) who teaches a method for the treatment of atherosclerosis in a patient suffering therefrom (col. 4, lines 22-25) which comprises (i) administering to said patient an effective amount of a psoralen compound, (ii) obtaining a portion, (a.k.a., an aliquot), of the patient's blood which is then subjected, *in vitro* (a.k.a. ex-vivo), to ultraviolet light in the UVA wavelength (col. 1, lines 57-68 and col. 2, lines 24-25); and (iii) returning said portion of the patient's blood back to the patient (col. 2, lines 1-4).

Bisaccia et al. fail to expressly disclose a "lipid profile modifying drug" or "a cholesterol-lowering drug". However, because atherosclerosis was known to be a condition associated with the accumulation of various lipids, such as low density lipoproteins (LDL) and cholesterol (see Merck Manual at page 386-387, under the heading "Pathology and Pathogenesis"); properly relied upon here to explain the meaning of the term "atherosclerosis" as used in the primary reference), and Bisaccia et al. teach the treatment of atherosclerosis, the psoralen compounds of Bisaccia et al. can be reasonably interpreted as being "lipid profile modifying" drugs given the plain meaning of the terms employed in the claimed expression "lipid profile modifying drug"

and that the atherosclerotic plaque in Stewart would be removed, thus lowering or otherwise modifying the patient's lipid and/or cholesterol level.

Claims must be given their broadest reasonable interpretation consistent with the supporting disclosure. See *In re Hyatt*, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Also, words and phrases in the claims must be given their "plain meaning" as understood by one having ordinary skill in the art unless defined by applicant in the specification with "reasonable clarity, deliberateness and precision". See MPEP § 2111.01. Here, Applicant has not defined the expressions "lipid modifying drug" or "cholesterol-lowering drug" and thus, the Examiner's interpretation is proper.

Suggestion for Overcoming the Above Rejection

In order to overcome the present rejection, Applicant should limit the "lipid modifying drug" or "cholesterol-lowering drug" to a statin drug as set forth in present claim 23.

Stewart (U.S. Patent No. 6,262,646) Does Not Teach or Suggest the Claimed Subject Matter

The present invention is generally directed methods for the treatment of atherosclerosis which comprise, *inter alia*, the step of administering to a subject an aliquot of the mammal's blood that has been treated ex-vivo with one or more stressors selected from the group consisting of oxidative stress, thermal stress and UV light, wherein a lipid profile modifying drug, e.g., a cholesterol-lowering drug, is also being administered to said subject.

Applicants have presented claims in Jepson format and the conventional style for defining a therapeutic method. Claims 1 and 42 are representative of the claimed invention and read as follows:

21. (New) In a method for treating a mammalian subject with a lipid profile modifying drug wherein the improvement comprises administering to the mammalian subject an aliquot of the mammal's blood that has been treated ex vivo with one or more stressors, selected from the group consisting of oxidative stress, thermal stress, and UV light.

42. (New) A method of slowing or arresting the progression and/or effecting the regression of atherosclerotic plaque deposits and/or improving the stability of such plaques in a mammalian patient, the method comprising administering to the patient a cholesterol modifying drug and an aliquot of the patient's own blood which has been treated ex vivo with one or more stressors, selected from the group consisting of an oxidative stress, thermal stress, and UV light.

The closest prior art is represented by Stewart (U.S. Patent No. 6,264,646) who teaches a method for delaying the onset, retarding the progression and causing regression of atherosclerosis in a mammal which comprises: (a) treating an aliquot of mammalian blood ex-vivo with at least one stressor selected from the group consisting of a temperature above or below body temperature, ultraviolet light and an oxidative environment; and (b) administering the aliquot of blood treated in step (a) to the mammal, wherein the aliquot has a volume sufficient to achieve a reduction in lipid levels in the mammal (see, for example, the abstract).

The difference between the above and the claimed subject matter lies in that a step of administering a lipid profile modifying drug, e.g., a cholesterol-lowering drug, in addition to the administration of the aliquot of blood is not disclosed.

However, the difference between the subject matter sought to be patented and the prior art is not such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. This is believed to be the case because Stewart further teaches away from the conventional means of treating atherosclerosis, such as the administration of a lipid profile modifying drug, e.g., a cholesterol-lowering drug, and as such, it is not believed that one of ordinary skill in the art would have been motivated to modify the invention as disclosed by Stewart in such a manner so as to arrive at the presently claimed subject matter.

At col. 1, lines 18-67, Stewart discusses the conventional treatment of atherosclerosis which involves the administration of cholesterol-lowering drugs and emphasizes that "[h]owever, drugs are not always warranted for hyperlipidemia, and some lipid-lowering drugs may have serious side effects.". Stewart further discloses that "[t]he present invention overcomes at least some of the above-noted and other disadvantages of presently known therapies for treatment of hyperlipidemia, such as hypercholesterolemia and elevated serum triglyceride levels, by providing a method for treating hyperlipidemia in which an aliquot of mammalian blood is treated ex vivo and subsequently introduced into the body of a mammalian subject.".

Accordingly, for the above reasons, the claimed subject matter is deemed to have not been obvious to one of ordinary skill in the art.

Claims 21-48 stand rejected.

Claims 23, 25, 32-41 and 45-47 are objected to.

The references cited on the attached form PTO-892 and not relied on are cited to show the general state of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

February 2, 2005